#10 Decl. w/attach 10/4/02

PC-0022 CIP

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Tang et al.

Title: GROWTH-RELATED INFLAMMATORY AND IMMUNE RESPONSE PROTEIN

Serial No.:	09/747,524	Filing Date:	December 19, 2000
Examiner:	Hill, M.	Group Art Unit:	1648

Commissioner for Patents
Washington DC 20231

DECLARATION UNDER 37 CFR 1.132 OF MICHAEL G. WALKER

I, Michael G. Walker, declare:

1. I received my doctoral degree from Stanford University, Stanford, CA in 1992. I have held the position of Consulting Professor in the Department of Medicine at Stanford University since 1995 and have consulted to Incyte Genomics since 1996. My work has involved the development of analytical tools for the characterization and annotation of molecules by their expression in relation to cellular function, disease, and metabolic pathways. I am an inventor on the pending application.

2. This application relates to an isolated polynucleotide encoding a growth-related inflammatory and immune response protein, GRIIP, and to the use of the polynucleotide in the diagnosis and treatment of cell immune disorders, in particular, cancers of the immune system. I understand that the Examiner has rejected claims 1-7 and 9 of this application for lack of a patentable utility and enablement.

3. The Examiner has stated in the Office Action that with regard to diagnosis or treatment of disease, the Examiner has stated that one skilled in the art would doubt the usefulness of the DNA (or protein) for the diagnosis or treatment of diseases or disorders associated with inflammation and the immune response because there is no guidance as to which diseases or disorders that there is a particular association because there is no showing in the specification that links a particular disease state to the presence of the cDNA. This declaration is provided to support a specific and substantial use of the claimed polynucleotides in the diagnosis of cancers of the immune system, in particular, bone marrow and

spleen cancers.

4. The diagnostic utility of the molecule is set forth in the specification at p. 3, lines 11-14;"The invention is based on the discovery of a mammalian cDNA which encodes a mammalian growth-related inflammatory and immune response protein (GRIIP) which is useful in the diagnosis and treatment of disorders associated with inflammation and immune response, particularly cancers of the immune system", and at p.17, line 33 trough p. 18, line 5; "The cDNAs, fragments, oligonucleotides, complementary RNA and DNA molecules, and PNAs and may be used to detect and quantify differential gene expression, absence/presence vs. excess, expression of mRNAs---". "Disorders associated with differential expression include disorders associated with inflammation and immune response, particularly cancers of the immune system".

5. Support for this use of the polynucleotide in the diagnosis or monitoring the treatment of disorders associated with inflammation and immune response, particularly cancers of the immune system, is found in the specification at pp. 9-10 and Figures 3A and 3B of the specification. Nucleic acids encoding GRIIP, were first identified, as described at p. 9 of the specification, as coexpressed with several known cell cycle specific genes through GBA analysis in USSN 09/229,253, referenced at p. 27, line 13 of the specification.. GRIIP was therefore identified as a growth-associated protein by these studies.

Figure 3A of the instant application further shows the predominate expression of polynucleotide encoding GRIIP in cells and tissues of the hemic and immune system. In particular, GRIIP was expressed in 15 of 159 libraries examined in that category. Figure 3B of the specification further shows that within the immune system category, SEQ ID NO:2 is expressed in several cancers of the immune system including; a bone marrow neuroblastoma (BMARXTXR02, -03, and -06); leukemia (TBLYNOT01); lymphoma (U937NOT01); chronic myelogenous leukemia (CML) (MYEPTXT01); and a spleen tumor (SPLNTUT02).

By way of explanation, I need clarify that criteria for data such as that shown in Figures 3A and 3B can be selected prior to running the analysis; the output may be run by category, number of cDNAs per library, library description, disease indication, clinical relevance, and so forth. cDNAs from more than 1538 libraries in the LIFESEQ Gold database have been categorized by organ, tissue, and cell type. For each category, the number of libraries in which the sequence was expressed were counted and shown over the total number of libraries in that category. In some analyses, all normalized or subtracted libraries, which have high copy number sequences removed prior to processing, and all mixed or pooled tissues, which are considered non-specific in that they contain more than one tissue type or more than one

subject's tissue, can be excluded from the analysis. Treated and untreated cell lines and/or fetal tissue data can also be removed where clinical relevance is of greatest importance. Conversely, fetal tissue may be purposely selected wherever elucidation of inherited disorders or differentiation of particular cells or organs from stem cells (i.e., nerves, heart or kidney) would be furthered by removing clinical samples.

Figure 3B represents all of the tissues from the 159 hemic and immune cell libraries examined in which SEQ ID NO:2 is expressed. Pooled, normalized and subtracted libraries (a total of 3) were excluded from the analysis for the reasons given above. As described at p. 9 of the specification, and Figure 3B, SEQ ID NO:2 was expressed in 7 immune cell libraries associated with cancer. These and other libraries listed in Figure 3B are described in detail in the attached Appendix I. Of particular note is the expression of GRIIP in a bone marrow cell line derived from a bone marrow tumor, a neuroblastoma, and a spleen tumor, as described above. Within the remaining hemic and immune cell libraries tested, GRIIP expression was not found in at least four bone marrow libraries unassociated with disease, i.e., BMARNOP01 BMARNOP02, BMARNOR02, and BMARNOT02. GRIIP expression was also not found in at least 7 adult spleen libraries unassociated with disease, e.g., SPLNNOE01, SPLNNOP01, SPLNNOP03, SPLNNOT02, SPLNNOT04, SPLNNOT13, and SPLNNOT17. GRIIP expression was found in only one other spleen library, SPLNFET02, a fetal tissue library as might be expected of a growth-associated, cell cycle gene. The association of GRIIP with bone marrow cancer has been further confirmed by its expression in an additional bone marrow tumor cell library, BMARUNP01, from the Mammalian Gene Collection of the National Cancer Institute who have independently reported the isolation of the gene encoding GRIIP from that source. See attached GenBank entry (Accession No. BC008489; Exhibit A)

When used in a tissue specific and clinically relevant manner, the expression of GRIIP in adult spleen and bone marrow is diagnostic of a cancer in these tissues.

I hereby declare that all statements made herein are true and that they are based on my own knowledge, information and belief. These statements are made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issued from it.

Date: 11 Sept 2002
9/11/02

Michael G. Walker

1050 Borregas Avenue #80
Sunnyvale, California 94089